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| 10/517,903 | 12/10/2004 | Michael G Willits | 70058USPCT | 4683 |

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| EXAMINER |
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ROBINSON, KEITH O NEAL

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| ART UNIT | PAPER NUMBER |
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1638

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| NOTIFICATION DATE | DELIVERY MODE |
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03/09/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/517,903 | Applicant(s) WILLITS ET AL. | |
| | Examiner KEITH O. ROBINSON | Art Unit 1638 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 37-53 is/are pending in the application.
- 4a) Of the above claim(s) 44-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action mailed June 17, 2009. Applicant's cancellation of claims 1-36, amendment of claim 37 and withdrawal of claims 44-53, filed November 6, 2009, have been received and entered in full.

Claims 37-43 are under examination.

Response to Arguments

Applicant's amendment of claim 37 citing the genes that must be present in the flesh of the tomato plant (see page 2 of 'Amendments to the claims' filed November 6, 2009) have overcome the 35 USC 112, second paragraph rejection on page 3 of the Office Action mailed June 17, 2009. The rejection has been withdrawn.

Claim Rejections - 35 USC § 103

Claims 37-43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Goffreda et al (Theor Appl Genet 78: 210-216, 1989), in view of Muir et al (Nature Biotechnology 19: 470-474, 2001), in view of Peralta et al (American J. Botany 88(10): 1888-1902, 2001), in view of Allard (Interspecific hybridization in plant breeding. *In* Principles of plant breeding, Chapter 34, pp. 434-443, 1960).

The claims read on a method of making a hybrid *Lycopersicon* plant expressing flavonol in the peel and flesh of the fruit of said plant by crossing a wild *Lycopersicon* species that expresses *CHI* in the peel and that expresses genes of the flavonol

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biosynthetic pathway in the flesh with a *L. esculentum* plant to produce said hybrid plant, wherein said genes of the flavonol biosynthetic pathway comprise CHS, CHI, F3H and FLS.

The claims read on an interspecific cross between two species of *Lycopersicon* wherein desirable genes from the wild *Lycopersicon* species is introgressed into the *L. esculentum* to produce a hybrid plant having the desired genes.

The state of the art teaches that interspecific crosses are used to improve tomato plants by introgressing desired genes from wild species of *Lycopersicon* into *L. esculentum*. Allard (Interspecific hybridization in plant breeding. *In* Principles of plant breeding, Chapter 34, pp. 434-443, 1960) teaches, “[i]nterspecific hybridization in the genus *Lycopersicon* is particularly interesting because many different hybrids can be secured, and most of the hybrids that can be made are sufficiently fertile to permit extensive studies of their progeny...[and] [h]ybrids of *L. esculentum* with *L. peruvianum* and the closely related species *L. chilense* hold the greatest promise of contributing useful traits to horticultural varieties of tomatoes”. See page 436, 1st paragraph, under section entitled “Interspecific hybridization of tomatoes” and page 437, last paragraph to page 438, line 1.

Therefore, it would have been obvious to one of ordinary skill in the art to use wild species of *Lycopersicon* in a cross with *L. esculentum* to produce hybrid plants that have a desired trait because Allard teaches that wild species are easily crossed with domesticated tomato and that wild species are used in crosses with domesticated tomato to contribute useful traits.

Goffreda et al teach a method of making a hybrid *Lycopersicon* plant by crossing a wild *Lycopersicon* species with a *L. esculentum* plant. See, for example, page 212, Table 2 where it teaches the cross of *L. esculentum* cv. New Yorker x *L. pennellii* LA716 and the cross of *L. esculentum* cv. VF Vendor x *L. pennellii* LA716 and the F1 hybrids produced from both crosses. In addition, Goffreda et al teach that hybrid plants produced from such a cross had the resistance gene of the wild *Lycopersicon* species. See, page 212, Table 2 and 2nd column, 1st paragraph of 'Results and discussion'.

Goffreda et al differs from the claimed invention in that Goffreda et al teach a wild *Lycopersicon* species that expresses potato aphid resistance and does not teach a wild *Lycopersicon* species that expresses *CHI* in the peel and that expresses genes of the flavonol biosynthetic pathway in the flesh.

Muir et al teach the importance of *CHI* in the flavonol biosynthetic pathway. See, for example, page 470, 1st column, last paragraph to 2nd column, lines 1-6 where it teaches that chalcone isomerase is an enzyme involved in flavonol biosynthesis and has been used to produce transgenic fruit with an increase in peel flavonols.

In addition, Muir et al teach the genes of the flavonol biosynthetic pathway (see, for example, page 471, Figure 1 where it teaches CHS, CHI, F3H and FLS) as well as the importance of the genes of the flavonol biosynthetic pathway (see, for example, page 470, 1st column, 2nd paragraph where it teaches "[f]lavonoids are...thought to possess health-promoting properties"). Furthermore, Muir et al teach that flavonoids occur naturally in fruits, vegetables, nuts, seeds and flowers (see page 470, 1st column, 2nd paragraph).

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Peralta et al teach accessions of wild *Lycopersicon* species, including LA1963, LA2884 and LA1926. See, for example, page 1890, Table 1. Thus, accessions of wild *Lycopersicon* species were known to those of ordinary skill in the art.

Therefore, it would have been obvious to one of ordinary skill in the art that the claimed method is a simple substitution of one known element for another to obtain a predictable result.

It would have been obvious to one of ordinary skill in the art to substitute the wild *Lycopersicon* species that expresses potato aphid resistance in the method of Goffreda with a wild *Lycopersicon* species that expresses *CHI* in the peel and that expresses genes of the flavonol biosynthetic pathway in the flesh as claimed in the instant invention. The results of the substitution would have been predictable because Allard teaches that wild species of *Lycopersicon* can be crossed with *L. esculentum* to produce hybrid plants that have a desired trait.

MPEP 2141 (I) teaches, "In KSR, the Supreme Court particularly emphasized "the need for caution in granting a patent based on the combination of elements found in the prior art,"Id. at ___, 82 USPQ2d at 1395, and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on its precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."Id. at ___, 82 USPQ2d at 1395...The Supreme Court further stated that:

When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a

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person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Id.* at ____, 82 USPQ2d at 1396”.

Thus, in the instant case, it would have been obvious to one of ordinary skill in the art that the method of Goffreda et al in producing hybrid tomato plants with potato aphid resistance by crossing a domesticated tomato with a wild species tomato having potato aphid resistance could be used to produce hybrid tomato plants to have flavonol in the peel and flesh of the fruit simply by crossing a domesticated tomato with a wild species tomato having *CHI* in the peel and that expresses genes of the flavonol biosynthetic pathway in the flesh.

Applicant argues that the Examiner's assertion that the claims read on an interspecific cross between two species of *Lycopersicon* wherein a desirable gene from the wild *Lycopersicon* species is introgressed into the *L. esculentum* to produce a hybrid plant having the desired gene is not an accurate statement of the claimed subject matter because the claims read on the introgression of specific genes from wild *Lycopersicon* species (see page 4, last paragraph to page 5, 1st paragraph of 'Remarks' filed November 6, 2009).

The Examiner acknowledges Applicant's remarks; however, even if the claims read on the introgression of specific genes from wild *Lycopersicon* species, the Allard references, as discussed in the previous Office Action mailed June 17, 2009, teaches

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interspecific hybridization in the genus of *Lycopersicon* and that hybrids produced from such crosses are fertile. Thus, it would have been obvious to one of ordinary skill in the art to introgress genes from wild *Lycopersicon* species. In addition, one of ordinary skill in the art would have been motivated to combine this teaching with that of the Muir reference to produce hybrid tomato plants that have genes of the flavonol biosynthetic pathway because the Muir reference teaches that “[f]lavonoids are...thought to possess health-promoting properties...[and] occur naturally in fruits, vegetables, nuts, seeds and flowers (see page 470, 1st column, 2nd paragraph).

Applicant argues that the Examiner has failed to provide a combination of references that includes each element of the claimed invention, namely (1) a wild *Lycopersicon* species expressing *CHI* in the peel and the genes of the flavonol biosynthetic pathway in the fruit flesh, (2) a domesticated *L. esculentum* plant, (3) crossing said wild and domesticated plant and (4) obtaining as a result a hybrid *Lycopersicon* plant that expresses *CHI* in the peel and the genes of the flavonol biosynthetic pathway in the fruit flesh (see page 5, 4th paragraph of 'Remarks' filed November 6, 2009).

This is not persuasive. With regard to (1), Peralta et al teach wild *Lycopersicon* species. Peralta et al do not teach wild *Lycopersicon* species expressing *CHI* in the peel and the genes of the flavonol biosynthetic pathway in the fruit flesh; however, Muir et al teach the importance of *CHI* in the flavonol biosynthetic pathway and by combining the Peralta and Muir references with the teachings of interspecific hybridization taught by

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Allard it would have been obvious to one of ordinary skill in the art to derive a wild *Lycopersicon* species expressing *CHI* in the peel and the genes of the flavonol biosynthetic pathway in the fruit flesh. Thus, it would have been obvious to one of ordinary skill in the art to substitute one known element for another to yield a predictable result. See MPEP 2143(B).

With regard to (2), Goffreda et al teach a *L. esculentum* plant. See, for example, page 212, Table 2 where it teaches the cross of *L. esculentum* cv. New Yorker.

With regard to (3) and (4), Goffreda et al teach crossing a wild *Lycopersicon* species with a *L. esculentum* plant. See, for example, page 212, Table 2 where it teaches the cross of *L. esculentum* cv. New Yorker x *L. pennellii* LA716 and the cross of *L. esculentum* cv. VF Vendor x *L. pennellii* LA716 and the F1 hybrids produced from both crosses and as discussed above, Muir et al teach the importance of *CHI* in the flavonol biosynthetic pathway; thus, by combining the Peralta and Muir references with the teachings of interspecific hybridization taught by Allard it would have been obvious to one of ordinary skill in the art to derive a wild *Lycopersicon* species expressing *CHI* in the peel and the genes of the flavonol biosynthetic pathway in the fruit flesh. Thus, it would have been obvious to one of ordinary skill in the art to substitute one known element for another to yield a predictable result. See MPEP 2143(B).

Applicant argues that the Muir reference only describes a transgenic approach to transferring *CHI* from *Petunia* into the peel only of a domesticated tomato and does not provide a method for transferring all genes of the biosynthetic pathway into the fruit

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flesh of a hybrid tomato plant as contemplated by the claimed invention via breeding techniques from wild *Lycopersicon* to *L. esculentum* (see page 5, last paragraph to page 6, line 3 of 'Remarks' filed November 6, 2009).

This is not persuasive. MPEP 2143(B) teaches that simple substitution of one known element for another to obtain predictable results is obvious. In the instant case, it would have been obvious to one of ordinary skill in the art that the wild *Lycopersicon* species used in a cross with *L. esculentum* to produce hybrid tomato as taught in the Goffreda et al reference can simply be substituted with the tomato plant taught in the Muir reference that expresses *CHI* in the peel to yield the predictable result of hybrid tomato plants that express *CHI* in the peel.

It would have been obvious to one of ordinary skill in the art to use the method of Goffreda et al in producing hybrid tomato plants having genes of the flavonol biosynthetic pathway by crossing a domesticated tomato with a wild species tomato because, as discussed above, Goffreda et al teach that hybrid plants produced from such a cross had the desired gene of the wild *Lycopersicon* species.

One of ordinary skill in the art would have been motivated to use a wild species tomato plant having genes of the flavonol biosynthetic pathway because the Muir reference teaches that flavonoids have been shown to exhibit a wide range of biological activities...including antioxidant and vasodilatory actions (see page 470, 1st column, 2nd paragraph).

With regard to the genes of the flavonol biosynthetic pathway cited in the newly amended claim 37, a person of ordinary skill has good reason to pursue the known

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options within his or her technical grasp. In the instant case, the genes of the flavonol biosynthetic pathway were known in the art, see, for example, page 471, Figure 1 of the Muir reference. Thus, it would have been obvious to one of ordinary skill in the art to select hybrid tomato plants having other genes in the flavonol biosynthetic pathway because the Muir reference teaches that flavonoids have been shown to exhibit a wide range of biological activities...including antioxidant and vasodilatory actions (see page 470, 1st column, 2nd paragraph).

Applicant argues that none of the cited references teach the importance of the genes of the flavonol biosynthetic pathway (*CHI*, *CHS*, *F3H*, *FLS*) or the transference of these genes into the fruit flesh of a wild *Lycopersicon* x *L. esculentum* hybrid tomato plant (see page 6, 1st full paragraph of 'Remarks' filed November 6, 2009).

This is not persuasive. The Muir reference teaches the genes of the flavonol biosynthetic pathway (see page 471, Figure 1) as well as the importance of the genes of the flavonol biosynthetic pathway (see, for example, page 470, 1st column, 2nd paragraph where it teaches "[f]lavonoids are...thought to possess health-promoting properties"). In addition, the Muir reference teaches that flavonoids occur naturally in fruits, vegetables, nuts, seeds and flowers (see page 470, 1st column, 2nd paragraph).

With regard to the transference of these genes into the fruit flesh of a wild *Lycopersicon* x *L. esculentum* hybrid tomato plant, the Goffreda reference teaches crossing a wild *Lycopersicon* species with a *L. esculentum* plant (see, for example, page 212, Table 2 where it teaches the cross of *L. esculentum* cv. New Yorker x *L.*

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pennellii LA716 and the cross of *L. esculentum* cv. VF Vendor x *L. pennellii* LA716 and the F1 hybrids produced from both crosses) and the Allard reference teaches that interspecific crosses are used to improve tomato plants by crossing wild species of *Lycopersicon* with *L. esculentum* (see, for example, page 436, 1st paragraph, under section entitled “Interspecific hybridization of tomatoes” and page 437, last paragraph to page 438, line 1).

These teachings combined with the Muir reference teaching of *CHI* in the flavonol biosynthetic pathway and the importance of flavonoids, as discussed above, would have been obvious to one of ordinary skill in the art because one of ordinary skill in the art would have been able to substitute one known element for another to yield a predictable result.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KEITH O. ROBINSON whose telephone number is (571)272-2918. The examiner can normally be reached Monday – Friday, 8:00 a.m. - 4:30 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Keith O. Robinson

/Anne Marie Grunberg/
Supervisory Patent Examiner, Art Unit 1638